Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1 – 14 (cancelled)

Claim 15 (withdrawn): A method of identifying genes in a eukaryotic genome, comprising:

algorithmically predicting at least one of said gene's exons from genomic sequence of said eukaryote; and then

detecting hybridization of mRNA-derived nucleic acids to a nucleic acid probe having a selectively hybridizable portion identical in sequence to, or complementary in sequence to, said predicted exon,

wherein said probe is included within a single exon microarray according to any one of claims 1 - 14.

Claim 16 (withdrawn): A method of measuring eukaryotic gene expression, comprising:

contacting the single exon microarray of any one of claims 1 - 14 with a first collection of detectably labeled nucleic acids, said first collection nucleic acids derived from mRNA of at least one eukaryotic tissue or cell type; and then

measuring the label detectably bound to each probe of said microarray.

Claim 17 (withdrawn): The method of claim 16, further comprising comparing said measurement to a second measurement, said second measurement identically obtained using a second, control, collection of nucleic acids.

Claim 18 (withdrawn): The method of claim 17, wherein said microarray is contacted simultaneously with said first and second collections of detectably labeled nucleic acids, wherein said first and second collection nucleic acids are distinguishably labeled.

Claim 19 (withdrawn): A visual display of eukaryotic genomic sequence annotated with information about a predetermined biologic function, comprising:

a first visual element, each point along the length of which first visual element maps linearly and uniquely to a nucleotide of said genomic sequence;

a second visual element, first and second boundaries of which second visual element map linearly to a first and second nucleotide of said genomic sequence, wherein said first and second nucleotides delimit a region of said genomic sequence predicted to have said predetermined function; and

a third visual element, first and second boundaries of which third visual element map linearly to a first and second nucleotide of said genomic sequence, wherein said first and second nucleotides delimit a region of said genomic sequence experimentally confirmed to have said predetermined function.

Claim 20 (withdrawn): The visual display of claim 19, wherein said display is electronic.

Claim 21 (withdrawn): A high throughput, microarray-based method to confirm predicted exons, comprising:

detecting hybridization by transcript-derived nucleic acids to microarray probes that include genomic sequence predicted to contribute to no more than one exon,

detectable hybridization confirming the prediction of the exon included in each of said detectably hybridized probes.

Claim 22 (withdrawn): The method of claim 21, wherein at least 75% of the probes of said microarray include genomic sequence predicted to contribute to no more than one exon.

Claim 23 (withdrawn): The method of claim 21, wherein at least 90% of the probes of said microarray include genomic sequence predicted to contribute to no more than one exon

Claim 24 (withdrawn): The method of claim 21, wherein at least 95% of the probes of said microarray include genomic sequence predicted to contribute to no more than one exon.

Claim 25 (withdrawn): The method of claim 21, wherein said genomic sequence is human genomic sequence.

Claim 26 (withdrawn): The method of claim 21, wherein said prediction is output from a computer program selected from the group consisting of GenScan, Diction, Genefinder, and Grail.

Claim 27 (withdrawn): The method of claim 26, wherein said prediction is output from GenScan.

Claim 28 (withdrawn): The method of claim 21, wherein said microarray has probes that collectively include exons predicted from all chromosomes of a eukaryotic organism.

Claim 29 (withdrawn): The method of claim 28, wherein said eukaryotic organism is a human being.

Claim 30 (withdrawn): The method of claim 21, wherein said microarray has probes that include exons predicted from human chromosome 22.

Claim 31 (withdrawn): The method of claim 21, wherein each of said predicted exons is represented by a plurality of probes on said array.

Claim 32 (withdrawn): The method of claim 21, wherein said microarray includes between 5,000 and 19,000 probes.

Claim 33 (withdrawn): The method of claim 21, wherein the genomic sequence included within said probes is selected at least in part based upon considerations of base composition and/or hybridization binding stringency.

Claim 34 (withdrawn): The method of claim 21, wherein said probes include at least 50 nt of predicted exon.

Claim 35 (withdrawn): The method of claim 21, wherein said probes include at least 75 nt of predicted exon.

Claim 36 (withdrawn): The method of claim 21, wherein said probes are amplified from genomic DNA.

Claim 37 (withdrawn): The method of claim 21, wherein said probes are chemically synthesized.

Claim 38 (withdrawn): The method of claim 21, wherein said probes are noncovalently attached to the substrate of said microarray.

Claim 39 (withdrawn): The method of claim 21, wherein said probes are covalently attached to the substrate of said microarray.

Claim 40 (withdrawn): The method of claim 21, wherein said probes are disposed on said microarray substrate by ink jet.

Claim 41 (withdrawn): The method of claim 21, wherein the substrate of said microarray is a glass slide.

Claim 42 (withdrawn): The method of claim 21, further comprising the antecedent step of:

contacting said microarray with at least a first sample of transcript-derived nucleic acids, said nucleic acids being detectably labeled.

Claim 43 (withdrawn): The method of claim 42, wherein said transcript-derived nucleic acids are first strand cDNA.

Claim 44 (withdrawn): The method of claim 43, wherein said cDNAs are fluorescently labeled.

Claim 45 (withdrawn): The method of claim 44, wherein said fluorescent label is selected from the group consisting of Cy3 and Cy5.

Claim 46 (withdrawn): The method of claim 42, wherein said contacting step comprises contacting said microarray concurrently with a first sample of transcript-derived nucleic acids and with a second sample of transcript-derived nucleic acids, wherein said first and second samples are labeled respectively with a first and a second label, said first and second labels being separately detectable.

Claim 47 (withdrawn): The method of claim 46, wherein said detecting includes normalizing and background correcting signals from each of said labels.

Claim 48 (withdrawn): The method of claim 46, wherein said labels are Cy3 and Cy5.

Claim 49 (withdrawn): The method of claim 46, wherein said first sample includes transcript-derived nucleic acids pooled from a plurality of tissues and/or cell types.

Claim 50 (withdrawn): The method of claim 49, wherein said pool includes transcript-derived nucleic acids from a plurality of human cell lines.

Claim 51 (withdrawn): The method of claim 49, wherein the transcript-derived nucleic acids of said second sample are derived from a cell line or normal tissue.

Claim 52 (withdrawn): The method of claim 51, wherein the transcript-derived nucleic acids of said second sample are derived from a source within the group of human tissues and cell lines consisting of: brain, heart, liver, fetal liver, placenta, lung, bone marrow, HeLa cells, BT474 cells and HBL 100 cells.

Claim 53 (withdrawn): A method of identifying potential false positive exon predictions, comprising:

detecting hybridization by transcript-derived nucleic acids to a microarray that has probes that include genomic sequence predicted to contribute to no more than one exon, absence of detectable hybridization identifying as a potential false positive the exon predicted in each undetectably hybridized probe.

Claim 54 (withdrawn): A method of identifying one or more genes expressed by one or more eukaryotic cells having a genome that averages at least one intron per gene, comprising:

(a) contacting a cDNA sample prepared by enzymatically copying messenger RNA obtained from said eukaryotic cell(s) into cDNA, wherein said cDNA comprises a detectable label, with a plurality of single exon probes, each said single exon probe comprising a discrete nucleic acid sequence encoding all or a portion of a single exon of said eukaryotic genome that specifically hybridizes at high stringency to a target nucleic acid when said target nucleic acid is present in said cDNA sample;

(b) detecting a signal from each said single exon probe that is specifically hybridized to said target nucleic acid, wherein the presence of said signal indicates the expression of a gene comprising said single exon by said eukaryotic cell(s).

Claim 55 (withdrawn): A method of identifying one or more genes expressed by one or more human cells, comprising:

(a) contacting a cDNA sample prepared by copying messenger RNA obtained from said human cell(s) into cDNA using reverse transcriptase, wherein said cDNA comprises a detectable label, with a nucleic acid microarray, said microarray comprising a substantially planar glass substrate comprising (i) at least 5000 addressable locations to which single exon probes are bound, each said single

exon probe comprising a discrete nucleic acid sequence encoding all or a portion of a single exon of a human genome that is specifically hybridizable at high stringency to a target nucleic acid, wherein said target nucleic acid is a sequence encoding all or a portion of an expressed gene, or a complementary sequence thereof, and (ii) one or more additional locations to which control nucleic acid sequences are bound; and

(b) generating a signal from each said addressable location, wherein the presence of a signal at a specific addressable location indicates the expression by said human cell(s) of a gene comprising the single exon probe bound to that addressable location.

Claim 56 (withdrawn): A high throughput, microarray-based method of grouping exons into a common gene, comprising:

comparing the patterns of tissue and/or cell-type expression of exons predicted from a contiguous region of genomic DNA,

wherein said patterns of expression have been determined by detecting hybridization of transcript-derived nucleic acids from a plurality of tissues and/or cell types to microarray probes, each of said probes including genomic sequence predicted to contribute to no more than one of said exons, said microarray including probes that collectively comprise all of said exons,

consensus in said expression patterns identifying exons that are groupable into a common gene.

Claim 57 (withdrawn): The method of claim 56, wherein said gene is a human gene.

Claim 58 (withdrawn): The method of claim 56, wherein said patterns are detected by detecting (i) fluorescence intensity, (ii) the ratio of intensity as between concurrently hybridized first and second samples, or (iii) a combination of (i) and (ii).

Claim 59 (withdrawn): A nucleic acid microarray comprising:

a substrate comprising a plurality of addressable locations to which nucleic acid sequences are bound; and

a plurality of single exon probes bound at said addressable locations, each said single exon probe comprising a discrete nucleic acid sequence encoding all or a portion of a single exon of a eukaryotic genome averaging at least one intron per gene that is specifically hybridizable at high stringency to a target nucleic acid, wherein said target nucleic acid is a sequence encoding all or a portion of an expressed gene, or a complementary sequence thereof.

Claim 60 (withdrawn): A nucleic acid microarray comprising:

a substantially planar glass substrate comprising (i) at least 5000 addressable locations to which single exon probes are bound, each said single exon probe comprising a discrete nucleic acid sequence encoding all or a portion of a single exon of a human genome that is specifically hybridizable at high stringency to a target nucleic acid,

wherein said target nucleic acid is a sequence encoding all or a portion of an expressed gene, or a complementary sequence thereof, and (ii) one or more additional locations to which control nucleic acid sequences are bound.

Claim 61 (currently amended): A single exon nucleic acid microarray, comprising:

a plurality of nucleic acid probes addressably disposed upon a substrate,

wherein each of said probes include genomic sequence of at least one predicted exon of a eukaryotic genome, at least 50% of said probes include genomic sequence of ~~predicted to contribute to~~ no more than one said exon of said ~~a~~ eukaryotic genome, said eukaryotic genome averaging at least one intron per gene, and wherein said plurality of nucleic acid probes averages at least 50 nt in length.

Claim 62 (previously presented): The microarray of claim 61, wherein at least 75% of said nucleic acid probes include genomic sequence predicted to contribute to no more than one exon of a eukaryotic genome.

Claim 63 (previously presented): The microarray of claim 61, wherein at least 90% of the probes of said microarray include genomic sequence predicted to contribute to no more than one exon of a eukaryotic genome.

Claim 64 (previously presented): The microarray of claim 61, wherein at least 95% of the probes of said microarray include genomic sequence predicted to contribute to no more than one exon of a eukaryotic genome.

Claim 65 (previously presented): The microarray of claim 61, wherein said microarray has probes that collectively include exons predicted from all chromosomes of a eukaryotic genome.

Claim 66 (previously presented): The microarray of claim 61, wherein said eukaryotic genome is a human genome.

Claim 67 (previously presented): The microarray of claim 65, wherein said eukaryotic genome is a human genome.

Claim 68 (currently amended): The microarray of claim 61, wherein said predicted exons within said probes are ~~prediction is~~ output from a computer program selected from the group consisting of GenScan, Diction, Genefinder, and Grail.

Claim 69 (currently amended): The microarray of claim 68, wherein said predicted exons within said probes are ~~prediction is~~ output from GenScan.

Claim 70 (previously presented): The microarray of claim 61, wherein each of said predicted exons is represented by a plurality of probes on said array.

Claim 71 (previously presented): The microarray of claim 61, wherein said microarray includes between 5,000 and 19,000 probes.

Claim 72 (currently amended): The microarray of claim 61, wherein the genomic sequence included within said probes is further selected ~~at least in part~~ based upon considerations of base composition and/or hybridization binding stringency.

Claim 73 (previously presented): The microarray of claim 61, wherein said probes have been amplified from genomic DNA.

Claim 74 (previously presented): The microarray of claim 61, wherein said probes have been chemically synthesized.

Claim 75 (previously presented): The microarray of claim 61, wherein said probes are noncovalently attached to the substrate of said microarray.

Claim 76 (previously presented): The microarray of claim 61, wherein said probes are covalently attached to the substrate of said microarray.

Claim 77 (previously presented): The microarray of claim 61, wherein said probes are disposed on said microarray substrate by ink jet.

Claim 78 (previously presented): The microarray of claim 61, wherein said substrate is a glass slide.

Claim 79 (previously presented): The microarray of claim 61, wherein each of said probes is disposed on said array with its reverse complement.

Claim 80 (currently amended): The microarray of claim 61, further comprising negative control probes for hybridization.

Claim 81 (currently amended): The microarray of claim 61, wherein at least 50% of said exon-including nucleic acid probes comprise, contiguous to a first end of said predicted exon, a first intronic and/or intergenic sequence that is identically contiguous to said exon

in said ~~the~~ eukaryotic genome, and further comprise, contiguous to a second end of said predicted exon, a second intronic and/or intergenic sequence that is identically contiguous to said exon in said ~~the~~ eukaryotic genome.

Claim 82 (withdrawn): A software data structure for annotating nucleic acid sequence with confirmed bioinformatic predictions, the data structure stored in a machine readable medium and comprising:

a plurality of sequence entries, each sequence entry including (i) a sequence identifier and (ii) software means for relating said sequence identifier to data that encode a confirmed prediction of a biological function of the nucleic acid sequence identified by said sequence identifier.

Claim 83 (withdrawn): The software data structure of claim 82, wherein said confirmed biological function is contribution to a mature mRNA transcript.

Claim 84 (withdrawn): The software data structure of claim 83, wherein said prediction is output from GenScan.

Claim 85 (withdrawn): The software data structure of claim 83, wherein said prediction has been confirmed by the method of claim 21.

Claim 86 (withdrawn): The software data structure of claim 82, wherein said software relating means is the common inclusion of said confirmed prediction data in a single record with said sequence identifier.

Claim 87 (withdrawn): The software data structure of claim 82, wherein said software relating means links said sequence identifier to confirmed prediction data present in a distinct record.

Claim 88 (withdrawn): The software data structure of claim 82, wherein said sequence entries further comprise:

software means for relating said sequence identifier to data that encode at least one nucleic acid sequence identified by said identifier.

Claim 89 (withdrawn): The software data structure of claim 88, wherein said sequence entries further comprise:

software means for relating said sequence identifier and/or said at least one nucleic acid sequence to data that encode a measure of similarity of the at least one nucleic acid sequence to at least one nucleic acid sequence prior-accessioned into a database.

Claim 90 (withdrawn): The software data structure of claim 89, wherein said sequence entries further comprise:

software means for relating said sequence identifier and/or said at least one nucleic acid sequence to data that encode a textual description of said at least one similar prior-accessioned nucleic acid sequence.

Claim 91 (withdrawn): The software data structure of claim 82, wherein said sequence entries further comprise:

software means for relating said sequence identifier to data that encode a chromosomal map location of the sequence identified by said sequence identifier.

Claim 92 (withdrawn): An isolated nucleic acid having exons that have been commonly grouped by the method of claim 56.

Claim 93 (previously presented): The microarray of claim 61, wherein said microarray includes at least 5,000 probes.

Claim 94 (previously presented): The microarray of claim 61, wherein said plurality of nucleic acid probes averages at least 100 bp in length.

Claim 95 (previously presented): The single exon nucleic acid microarray of claim 61, wherein at least 50% of said exon-including nucleic acid probes further comprise, contiguous to a first end of said predicted exon, a first intronic and/or intergenic sequence that is identically contiguous to said exon in the genome.

Claim 96 (previously presented): The single exon nucleic acid microarray of claim 61, wherein at least 95% of said exon-including nucleic acid probes further comprise, contiguous to a first end of said predicted exon, a first intronic and/or intergenic sequence that is identically contiguous to said exon in the genome.

Claim 97 (previously presented): The single exon nucleic acid microarray of claim 61, wherein at least 95% of said exon-including nucleic acid probes comprise, contiguous to a first end of said predicted exon, a first intronic and/or intergenic sequence that is identically contiguous to said exon in the genome, and further comprise, contiguous to a second end of said predicted exon, a second intronic and/or intergenic sequence that is identically contiguous to said exon in the genome.

Claim 98 (previously presented): The single exon nucleic acid microarray of claim 61, wherein at least 50% of said exon-including nucleic acid probes lack prokaryotic and bacteriophage vector sequence.

Claim 99 (previously presented): The single exon nucleic acid microarray of claim 61, wherein at least 95% of said exon-including nucleic acid probes lack prokaryotic and bacteriophage vector sequence.

Claim 100 (previously presented): The single exon nucleic acid microarray of claim 61, wherein at least 50% of said exon-including nucleic acid probes lack homopolymeric stretches of A or T.

Claim 101 (previously presented): The single exon nucleic acid microarray of claim 61, wherein at least 95% of said exon-including nucleic acid probes lack homopolymeric stretches of A or T.

Claim 102 (previously presented): The microarray of claim 61, wherein said eukaryotic genome averages at least two introns per gene.

Claim 103 (previously presented): The microarray of claim 61, wherein said eukaryotic genome averages at least three introns per gene.

Claim 104 (previously presented): The microarray of claim 61, wherein said eukaryotic genome averages at least five introns per gene.